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N-acetylcysteine: A Possible Treatment for Hairpulling in Trichotillomania

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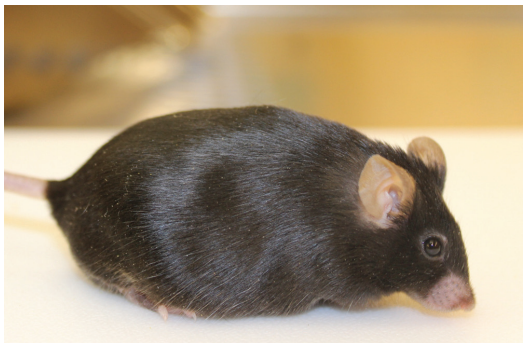
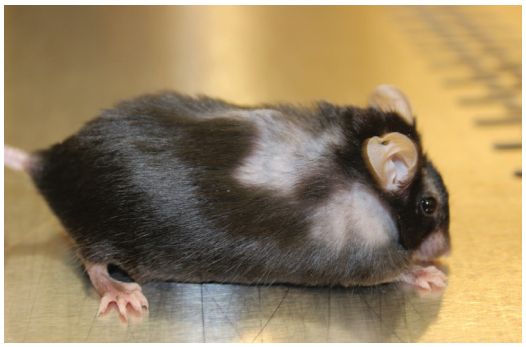
Trichotillomania (TTM) is a body-focused repetitive disorder found in approximately 4% of women. Patients pluck patches of hair, causing depression and anxiety. The most effective treatment is *N*-acetylcysteine (NAC), which is a precursor to glutathione, a fundamental antioxidant that protects the brain from reactive oxygen species (ROS). ROS accumulate through metabolism, widely damaging lipids, DNA, and proteins. Our objective is to study the effects of NAC in mice to understand etiology, identify biomarkers, and develop effective treatments. We hypothesize that increased metabolism causes an imbalance in oxidative stress, leading to cellular quiescence that manifests as barbering, a validated mouse model of TTM. We tested this by determining the ability of NAC (1g/kg/day) to prevent and cure barbering in ($N = 32$) C57BL/6 mice. We measured hairloss biweekly and determined oxidative stress levels by independent measures in urine, blood, and the brain. Using logistic regression, we discovered that barbering animals had elevated urinary antioxidant capacity ($P < 0.0001$) and increased levels of oxidized DNA ($P = 0.0439$). NAC protects and cures mice ($P = 0.0145$), and most importantly, oxidative stress at baseline predicted which animals would respond to NAC ($P = 0.0226$). Our data suggest a compensatory response to oxidative stress, confirm a relationship between oxidative stress and barbering, and provide a potential, highly effective treatment for TTM in mice and humans. Currently, we are conducting transcriptome studies to identify the genetic pathways that are disrupted in barbering animals and testing urine-based biomarkers in blood and the brain. We will use this information to design therapies to treat TTM in the human population.

Research advisor Professor Amy C. Lossie says, "Anusorn used behavioral, molecular, and genetic approaches to understand the etiology of trichotillomania, addressing the question, 'Why do some sisters become ill, and others not?' The results pinpointed oxidative stress in the pathophysiology of hairpulling in mice, delineated several predictive biomarkers, and identified an astoundingly effective nutraceutical therapy for prevention."



A normal female C57BL/6 mouse, 20 weeks of age, healthy, and no barbering behavior.



A barbering female C57BL/6 mouse, 20 weeks of age. The patches on her body indicating that she was over-groomed by her barbering cage mate and herself.

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